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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,925	03/10/2004	Wumin Li	AM 101333	3270

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EXAMINER	
TONGUE, LAKIA J	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
09/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/796,925	LI ET AL.	
	Examiner	Art Unit	
	LAKIA J. TONGUE	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 1, 2008 has been entered.

Applicant's response filed on August 1, 2008 is acknowledged. Claim 22 has been amended. Claims 22-24 are pending and under examination.

Objections Withdrawn

1. In view of Applicant's amendment, the objection to the claims for the acronym "SP oil" is withdrawn.

Rejections Withdrawn

2. In view of Applicant's amendment, the rejection of claims 22-24 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The rejection of claims 22 and 24 under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. (Effect of dairy calves with an inactivated *E. coli* O157:H7 bacterin on shedding of *E. coli* O157:H7, 1999; Abstract 40 aP), Saito et al. (U.S. 2005/0158330 A1), and Baylor et al. (Vaccine, 2002; 20: S18-S23) is maintained for the reasons set forth in the previous office action.

Applicant argues that:

1) None of the cited references, alone or in combination with one another, teach or suggest an oil emulsion comprising the ingredients recited in claim 22.

2) Johnson refers to an inactivated *E. coli* O157:H7 bacterin supplemented with inactivated intimin O157.

3) A person of ordinary skill in the art would have no reason to select from Saito any of the particular ingredients recited in the present claims, much less the precise combination of ingredients recited in the claims.

4) Baylor does not cure the aforementioned deficiencies of Johnson and/or Saito.

5) MPEP 2143 sets out seven different exemplary rationales that may support a conclusion of obviousness. None of the exemplary rationales apply to the currently claimed invention

Applicant's arguments have been considered, but are not persuasive.

The rejected claims are drawn to a method for reducing shedding of *E. coli* O157:H7 in an animal which comprises administering by parenteral injection to the animal an effective amount of a vaccine composition, wherein the vaccine composition comprises inactivated or killed *E. coli* O157:H7, an adjuvant and aluminum hydroxide, and optionally a pharmaceutically acceptable carrier; wherein said adjuvant is an oil emulsion comprising:

a) 1% to 3% vol/vol of polyoxyethylene-polyoxypropylene block copolymer;

b) 2% to 6% vol/vol of squalene;

c) 0.1% to 0.5% vol/vol of polyoxyethyene sorbitan monooleate; and

d) buffered salt solution.

With regard to Point 1, contrary to Applicant's arguments, the combination of references renders the instant composition obvious because they both teach the combination of components as claimed (i.e. components (a)-(d) and an aluminum hydroxide). Johnson et al. disclose a study to determine the effect of vaccinating dairy claves with an inactivated *Escherichia coli* O157:H7 bacterin on the shedding of Escherichia *coli* O157:H7 (see title). Johnson et al. disclose that six newly weaned calves were vaccinated intramuscularly with an inactivated *E. coli* O157:H7 bacterin.

Johnson et al. disclose that the shedding of the organism by most calves in each group fell to 50 CFU/g of feces within 2-3 weeks of challenge (see abstract).

Moreover, Saito et al. disclose oil adjuvant vaccines which include sorbitan fatty acid ester (e.g., sorbitan monooleate, etc.), non-ionic surfactants, having a polyoxyethylene chain in a molecule, such as polyoxyethylene sorbitan fatty acid ester polysorbate (e.g., polyoxyethylene(20)sorbitan monooleate etc.), polyoxyethylene polyoxypropylene glycol and the like (see paragraph 0034). Saito et al. disclose that the vaccine comprise antigens of inactivated cells from Gram negative bacteria such as *Escherichia coli* (see paragraph 0044). Moreover, the vaccine may contain, in addition to an antigen, an efficacious component such as an antibiotic (see paragraph 0045). Saito et al. disclose that suitable administration routes include subcutaneous, intramuscular and intraperitoneal injections (see paragraph 0066). Lastly, Saito et al. disclose using aluminum hydroxide in the disclosed composition (see paragraphs 0101 and 0109). Moreover, it would have been obvious to use the components together along with aluminum hydroxide because aluminum hydroxide is a known adjuvant that is well known in the art to stimulate an immune response.

Limitations such as the amount of each component of the oil emulsion are being viewed as limitations of optimizing experimental parameters.

With regard to Point 2, the instant claim recite open claim language and thus does not exclude other materials (i.e. inactivated verotoxin 2 and intimin O157) from being present in the claimed composition. Moreover, Johnson et al. disclose that shedding of the organism by most calves in each group fell to <50 CFU/g of feces within

2-3 weeks of challenge, thus meeting the limitation of reducing shedding of *E. coli* O157:H7 in an animal and meeting the requirement of a reasonable expectation of success.

With regard to Point 3, contrary to Applicants assertion, It would have been expected, barring evidence to the contrary, that the composition would be effective in reducing shedding of *E. coli* O157:H7 because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention (KSR International Co. v. Teleflex inc., 500 U.S.-, 82 US{Q2d 1385 (2007). Moreover, KSR forecloses the argument that a **specific** teaching, suggestion, or motivation is required to support a finding of obvious. See the recent Board decision *Ex parte Smith,--USPQ2d--,* slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR, 82 USPQ2d* at 1396).

With regard to Point 4, contrary to Applicant's arguments, Baylor et al., was used solely as an evidentiary reference to demonstrate that aluminum hydroxide has been commonly used as an adjuvant in many vaccines for decades and have been proven safe.

As previously presented, Johnson et al. disclose a study to determine the effect of vaccinating dairy claves with an inactivated *Escherichia coli* O157:H7 bacterin on the shedding of Escherichia *coli* O157:H7 (see title). Johnson et al. disclose that six newly weaned calves were vaccinated intramuscularly with an inactivated *E. coli* O157:H7

bacterin. Moreover, Johnson et al. disclose that the shedding of the organism by most calves in each group fell to 50 CFU/g of feces within 2-3 weeks of challenge (see abstract).

Johnson et al. does not specifically disclose an adjuvant comprising SP oil and aluminum hydroxide.

Saito et al. disclose oil adjuvant vaccines which include sorbitan fatty acid ester (e.g., sorbitan monooleate, etc.), non-ionic surfactants, having a polyoxyethylene chain in a molecule, such as polyoxyethylene sorbitan fatty acid ester polysorbate (e.g., polyoxyethylene(20)sorbitan monooleate etc.), polyoxyethylene polyoxypropylene glycol and the like (see paragraph 0034). Saito et al. disclose that the vaccine comprise antigens of inactivated cells from Gram negative bacteria such as *Escherichia coli* (see paragraph 0044). Moreover, the vaccine may contain, in addition to an antigen, an efficacious component such as an antibiotic (see paragraph 0045). Saito et al. disclose that suitable administration routes include subcutaneous, intramuscular and intraperitoneal injections (see paragraph 0066).

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Johnson et al. with the teachings of Saito et al. because Saito et al. disclose a vaccine which comprises inactivated cells of *E. coli* antigen coupled with an adjuvant comprising the components of SP oil. Further, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Johnson et al. with the teachings of Saito et al. to use inactivated whole *E. coli* O157:H7 because it is highly potent and can cause severe infections. It

would have been obvious to use the components together along with aluminum hydroxide because aluminum hydroxide is a known adjuvant that is well known in the art to stimulate an immune response. As evidenced by Baylor et al., which disclose that aluminum hydroxide has been commonly used as an adjuvant in many vaccines for decades and have been proven safe (see abstract and page S21-Summary).

It would have been expected, barring evidence to the contrary, that the composition would be effective in reducing shedding of *E. coli* O157:H7 because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention (KSR International Co. v. Teleflex inc., 500 U.S.-, 82 US{Q2d 1385 (2007). Moreover, KSR forecloses the argument that a **specific** teaching, suggestion, or motivation is required to support a finding of obvious. See the recent Board decision *Ex parte Smith,--USPQ2d--*, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR, 82 USPQ2d* at 1396).

The method of the prior art is the same as that which has been claimed, consequently, the method necessarily produces minimal injection site reaction.

4. The rejection of claims 22-24 under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. (Effect of dairy calves with an inactivated *E. coli* O157:H7 bacterin on shedding of *E. coli* O157:H7, 1999; Abstract 40 aP), in view of Saito et al. (U.S. 2005/0158330 A1), in view of Baylor et al. (Vaccine, 2002; 20: S18-S23) as set forth

above and further in view of Elder et al. (Journal of Animal Science, 2002; 80 (sup. 1): 151 (abstract 602)).

Applicant argues that:

1) None of the cited references, alone or in combination with one another, teach or suggest an oil emulsion comprising the ingredients recited in claim 22.

2) Johnson refers to an inactivated *E. coli* O157:H7 bacterin supplemented with inactivated intimin O157.

3) A person of ordinary skill in the art would have no reason to select from Saito any of the particular ingredients recited in the present claims, much less the precise combination of ingredients recited in the claims.

4) Baylor does not cure the aforementioned deficiencies of Johnson and/or Saito.

5) MPEP 2143 sets out seven different exemplary rationales that may support a conclusion of obviousness. None of the exemplary rationales apply to the currently claimed invention.

6) Elder does not cure any of the noted deficiencies of Johnson, Saito and/or Baylor.

Applicant's arguments have been considered, but are not persuasive.

The rejected claims are drawn to a method for reducing shedding of *E. coli* O157:H7 in an animal which comprises administering by parenteral injection to the animal an effective amount of a vaccine composition, wherein the vaccine composition comprises inactivated or killed *E. coli* O157:H7, an adjuvant and aluminum hydroxide,

and optionally a pharmaceutically acceptable carrier; wherein said adjuvant is an oil emulsion comprising:

a) 1% to 3% vol/vol of polyoxyethylene-polyoxypropylene block copolymer;

b) 2% to 6% vol/vol of squalene;

c) 0.1% to 0.5% vol/vol of polyoxyethyene sorbitan monooleate; and

d) buffered salt solution.

Subsequent claim 23 is drawn to a method that further comprises administering an effective amount of *Lactobacillus acidophilus* or neomycin medicated feed supplement to the animal.

With regard to Point 1, contrary to Applicant's arguments, the combination of references renders the instant composition obvious because they both teach the combination of components as claimed (i.e. components (a)-(d) and an aluminum hydroxide). Johnson et al. disclose a study to determine the effect of vaccinating dairy claves with an inactivated *Escherichia coli* O157:H7 bacterin on the shedding of Escherichia *coli* O157:H7 (see title). Johnson et al. disclose that six newly weaned calves were vaccinated intramuscularly with an inactivated *E. coli* O157:H7 bacterin. Johnson et al. disclose that the shedding of the organism by most calves in each group fell to 50 CFU/g of feces within 2-3 weeks of challenge (see abstract).

Moreover, Saito et al. disclose oil adjuvant vaccines which include sorbitan fatty acid ester (e.g., sorbitan monooleate, etc.), non-ionic surfactants, having a polyoxyethylene chain in a molecule, such as polyoxyethylene sorbitan fatty acid ester polysorbate (e.g., polyoxyethylene(20)sorbitan monooleate etc.), polyoxyethylene

polyoxypropylene glycol and the like (see paragraph 0034). Saito et al. disclose that the vaccine comprise antigens of inactivated cells from Gram negative bacteria such as *Escherichia coli* (see paragraph 0044). Moreover, the vaccine may contain, in addition to an antigen, an efficacious component such as an antibiotic (see paragraph 0045). Saito et al. disclose that suitable administration routes include subcutaneous, intramuscular and intraperitoneal injections (see paragraph 0066). Lastly, Saito et al. disclose using aluminum hydroxide in the disclosed composition (see paragraphs 0101 and 0109). Moreover, it would have been obvious to use the components together along with aluminum hydroxide because aluminum hydroxide is a known adjuvant that is well known in the art to stimulate an immune response.

Limitations such as the amount of each component of the oil emulsion are being viewed as limitations of optimizing experimental parameters.

With regard to Point 2, the instant claim recite open claim language and thus does not exclude other materials (i.e. inactivated verotoxin 2 and intimin O157) from being present in the claimed composition. Moreover, Johnson et al. disclose that shedding of the organism by most calves in each group fell to <50 CFU/g of feces within 2-3 weeks of challenge, thus meeting the limitation of reducing shedding of *E. coli* O157:H7 in an animal and meeting the requirement of a reasonable expectation of success.

With regard to Points 3 and 5, contrary to Applicants assertion, It would have been expected, barring evidence to the contrary, that the composition would be effective in reducing shedding of *E. coli* O157:H7 because all the claimed elements were known

in the prior art and one skilled in the art could have combined the elements as claimed with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention (KSR International Co. v. Teleflex inc., 500 U.S.-, 82 US{Q2d 1385 (2007). Moreover, KSR forecloses the argument that a **specific** teaching, suggestion, or motivation is required to support a finding of obvious. See the recent Board decision *Ex parte Smith,--USPQ2d--,* slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR, 82 USPQ2d* at 1396).

With regard to Point 4, contrary to Applicant's arguments, Baylor et al., was used solely as an evidentiary reference to demonstrate that aluminum hydroxide has been commonly used as an adjuvant in many vaccines for decades and have been proven safe.

With regard to Point 6, contrary to Applicant's assertion, Elder et al. disclose an intervention to reduce fecal shedding of *E. coli* O157:H7 in naturally infected cattle when administered neomycin (see page 151, abstract 602). Moreover, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the teachings of Johnson et al., Saito et al., and Baylor et al. with the teachings of Elder et al. because it is obvious to combine two compositions (neomycin and inactivated or killed whole *E. coli* O157:H7) each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850,205 USPQ 1069, 1072 (CCPA 1980).

Providing the composition as a medicated feed would be obvious because it provides a more convenient means of delivery and would be more suitable for the improvement of intestinal function when fed to dairy animals such as cows, goats and ewes.

As previously presented, Johnson et al., Saito et al., and Baylor et al. disclose the limitations of claims 22 and 24 above. Johnson et al., Saito et al., and Baylor et al. do not specifically disclose that the method further comprises administering an effective amount of *Lactobacillus acidophilus* or neomycin medicated feed to the animal.

As set forth above, Johnson et al. disclose a study to determine the effect of vaccinating dairy claves with an inactivated *Escherichia coli* O157:H7 bacterin on the shedding of Escherichia *coli* O157:H7 (see title). Johnson et al. disclose that six newly weaned calves were vaccinated intramuscularly with an inactivated *E. coli* O157:H7 bacterin. Moreover, Johnson et al. disclose that the shedding of the organism by most calves in each group fell to 0 CFU/g of feces within 2-3 weeks of challenge (see abstract).

Johnson et al. does not specifically disclose an adjuvant comprising SP oil and aluminum hydroxide or the optional pharmaceutically acceptable carrier.

Saito et al. disclose oil adjuvant vaccines which include sorbitan fatty acid ester (e.g., sorbitan monooleate, etc.), a non-ionic surfactant, having a polyoxyethylene chain in a molecule, such as polyoxyethylene sorbitan fatty acid ester polysorbate (e.g., polyoxyethylene(20)sorbitan monooleate etc.), polyoxyethylene polyoxypropylene glycol and the like (see paragraph 0034). Saito et al. disclose that the vaccine comprises antigens of inactivated cells from Gram negative bacteria such as *Escherichia coli* etc.

(see paragraph 0044). The vaccine may contain, in addition to an antigen, an efficacious component such as an antibiotic (see paragraph 0045). Moreover, Saito et al. disclose that suitable administration routes include subcutaneous, intramuscular and intraperitoneal injections (see paragraph 0066).

Saito et al. do not specifically disclose the use of aluminum hydroxide.

Elder et al. disclose an intervention to reduce fecal shedding of *E. coli* O157:H7 in naturally infected cattle when administered neomycin (see page 151, abstract 602).

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the teachings of Johnson et al., Saito et al., and Baylor et al. with the teachings of Elder et al. because it is obvious to combine two compositions (neomycin and inactivated or killed whole *E. coli* O157:H7) each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850,205 USPQ 1069, 1072 (CCPA 1980). Providing the composition as a medicated feed would be obvious because it provides a more convenient means of delivery and would be more suitable for the improvement of intestinal function when fed to dairy animals such as cows, goats and ewes.

It would have been expected, barring evidence to the contrary, that the composition would be effective because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed with no change in their respective functions, and the combination would have yielded

predictable results to one of ordinary skill in the art at the time of the invention (KSR International Co. v. Teleflex inc., 500 U.S.-, 82 US{Q2d 1385 (2007). Moreover, KSR forecloses the argument that a **specific** teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith,--USPQ2d--,* slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR, 82 USPQ2d* at 1396).

Conclusion

5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKIA J. TONGUE whose telephone number is (571)272-2921. The examiner can normally be reached on Monday-Friday 8-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LJT
9/8/08

/Robert A. Zeman/

for Lakia J. Tongue, Examiner of Art Unit 1645